

Notice of Allowability

Application No.

09/998,130

Examiner

Louise N. Leary

Applicant(s)

KISHIMOTO ET AL.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to amendment filed 8-10-2004.
2. ☒ The allowed claim(s) is/are 7-18 and 21-81.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

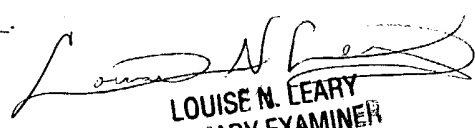
Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date 12-03;6-04
4. ☐ Examiner's Comment Regarding Requirement for Deposit
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413),
Paper No./Mail Date _____.
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.


LOUISE N. LEARY
PRIMARY EXAMINER

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

In the claims:

In claim 8, line 2, change "glutathionde-dependent" to ---glutathione-dependent---.

In claim 49, line 1, change "Glutathione-dependent formaldehyde dehydrogenase" to ---An isolated glutathione-dependent formaldehyde dehydrogenase (EC 1.2.1.2)---.

In claim 54, line 1, change "Dimethylglycine oxidase" to ---An isolated dimethylglycine oxidase (EC 1.5.3.10)---.

In the specification:

Delete the current "ABSTRACT OF THE DISCLOSURE", and insert

---ABSTRACT OF THE DISCLOSURE---

The present invention provides novel glutathione-dependent formaldehyde dehydrogenase that makes possible quantitative measurement of formaldehyde by cycling reaction, and a determination method of formaldehyde and biological components, such as creatinine, creatine, and homocysteine, which produces

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formaldehyde as a reaction intermediate. In addition, the present invention provides a reagent kit for the above-mentioned determination method. The present invention provides a novel determination method of a homocysteine using transferase utilizing homocysteine and other compound as a pair of substrates. Particularly, the present invention provides a determination method of homocysteine which includes bringing betaine-homocysteine methyltransferase and dimethylglycine oxidase into contact with a sample and measuring produced hydrogen peroxide or formaldehyde. Moreover, the present invention provides novel dimethylglycine oxidase stable to thiol compound, which is suitably used for the measurement. The present invention provides a reagent kit used for any of the above-mentioned determination methods of homocysteine.---

2. The following is an examiner's statement of reasons for allowance:

The reasons for allowance of the claims is that none of the prior art of record disclose or suggest (I) method for determining formaldehyde that comprises the steps of (a) bringing glutathione-dependent formaldehyde dehydrogenase having an optimal pH of about 7.5 to 8.5 and having a ratio of reactivity with thio-NAD to reactivity with NAD of not less than 0.3, glutathione and an oxidized coenzyme into contact with a sample, and analyzing a compound resulting from the enzymatic reaction, wherein the glutathione-dependent formaldehyde dehydrogenase is derived from *Hansenula nonfermentans* IFO1473; (II) a method for determining formaldehyde which comprises bringing glutathione-dependent formaldehyde dehydrogenase having a ratio of reactivity with thio-NAD to reactivity with NAD of not less than 0.3, glutathione, one compound

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selected from the group consisting of reduced thio-NADs and reduced thio-NADPs, and one compound selected from the group consisting of NADs and NADPs into contact with a sample to allow cycling reaction and analyzing changes in the amount of a compound due to the reaction; (IV) a method for determining homocysteine which comprises bringing a transferase utilizing homocysteine and another compound as a pair of substrates and said another compound into contact with a sample and measuring the resulting compound and wherein the transferase and another compound is in a combination selected from the group consisting of betaine-homocysteine methyltransferase and betaine, betaine-homocysteine methyltransferase and dimethylthein, homocysteine methyltransferase and S-adenosylmethionine, and N5-methyltetrahydrofolate-homocysteine methyltransferase and N5-methyltetrahydrofolate, and the resulting compound is methionine, and wherein the betaine, betaine-homocysteine methyltransferase, dimethylglycine oxidase and, where necessary, sarcosine oxidase are brought into contact with a sample, hydrogen peroxide produced by the enzymatic reactions is reacted with hydrogen donor chromogenic reagent and where necessary, coupler, in the presence of peroxidase, and the resulting pigment is measured; (V) an isolated glutathione-dependent formaldehyde dehydrogenase (EC1.2.1.1) having the physio-chemical properties claimed in the present invention; (VI) an isolated dimethylglycine oxidase (EC 1.5.3.10) having the physio-chemical properties claimed in the present invention; (VII) a reagent kit for determining formaldehyde comprising at least a buffer, glutathione, glutathione-dependent formaldehyde dehydrogenase (EC1.2.1.1), and a reagent for analyzing a compound

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produced by the enzymatic reaction; (VIII) a reagent kit for formaldehyde determination comprising at least a buffer, glutathione, glutathione-dependent formaldehyde dehydrogenase (EC1.2.1.1), one compound selected from the group consisting of thio-NADs and thio-NADPs, and one compound selected from the group consisting of reduced NADs and reduced NADPs; (IX)) a reagent kit for formaldehyde determination comprising at least a buffer, glutathione, glutathione-dependent formaldehyde dehydrogenase (EC1.2.1.1), one compound selected from the group consisting of thio-NADs and thio-NADPs, and one compound selected from the group consisting of NADs and NADPs; (X) a reagent kit for homocysteine determination comprising a buffer, transferase utilizing homocysteine and another compound as a pair of substrates, and a reagent for analyzing a compound produced by a reaction of the transferase utilizing homocysteine and the another compound as substrates; (XI) a reagent kit for homocysteine determination comprising a buffer, betaine, betaine-homocysteine methyltransferase, dimethylglycine oxidase, and a reagent for measuring hydrogen peroxide produced by the enzymatic reaction; nor (XII) a reagent kit for homocysteine determination comprising a buffer, betaine, betaine-homocysteine methyltransferase, dimethylglycine oxidase, and a reagent for determination of formaldehyde produced by the enzymatic reactions as claimed in the present invention.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably

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accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise N. Leary whose telephone number is (571)272-0966. The examiner can normally be reached on Monday to Friday from 9:30 to 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on (571)272-0974. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Louise N. Leary
Primary Examiner
Art Unit 1654
September 30, 2004